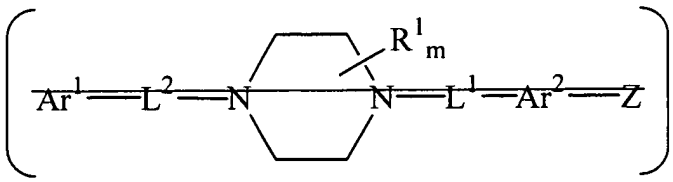
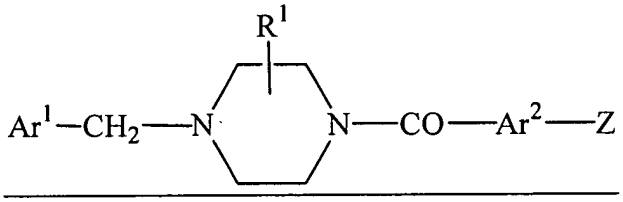
CLAIM AMENDMENTS

1. (currently amended): A compound of the formula:





or the pharmaceutically acceptable salts thereof, or a pharmaceutical composition thereof, wherein:

Ar^1 is an aryl group substituted with 0-5 non-interfering substituents~~, wherein two adjacent noninterfering substituents can form a fused aromatic or nonaromatic ring~~ selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, NH-aroyl, halo, OR, NR_2, SR, SOR, SO_2R, OCOR, NRCOR, $NRCONR_2$, NRCOOR, $OCONR_2$, RCO, COOR, alkyl-OOCR, SO_3R, $CONR_2$, SO_2NR_2, $NRSO_2NR_2$, CN, CF_3, R_3Si, and NO_2, wherein each R is independently H, alkyl, alkenyl or aryl or heteroforms thereof, and wherein two of said optional substituents on adjacent positions can be joined to form a fused, optionally substituted aromatic or nonaromatic, saturated or unsaturated ring which contains 3-8 members;

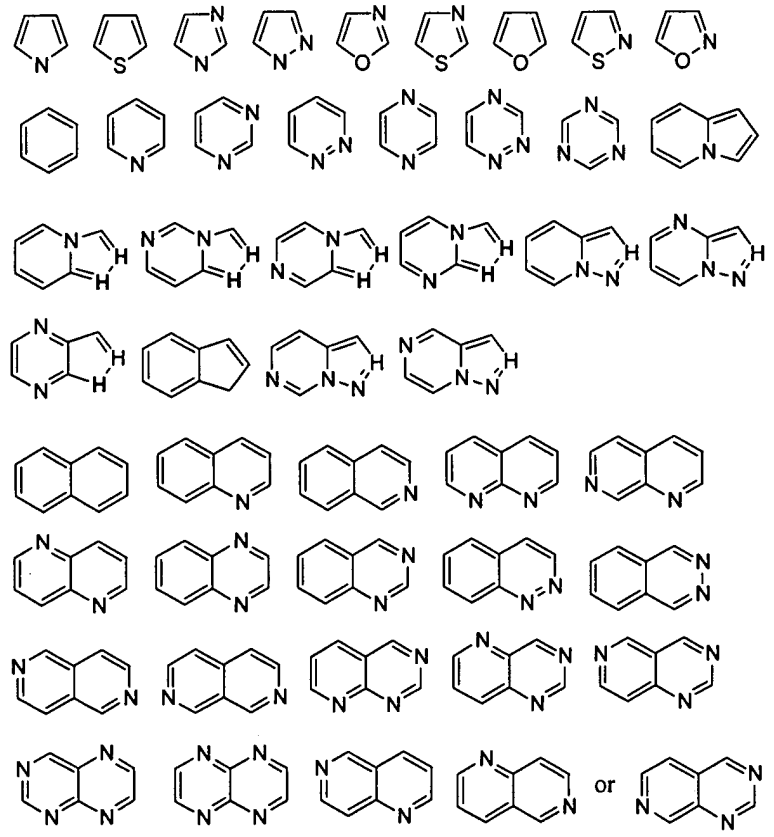
~~L^1 and L^2 are linkers;~~

each R^1 is independently a noninterfering substituent selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, NH-aroyl, halo, OR, NR_2, SR, SOR, SO_2R, OCOR, NRCOR, $NRCONR_2$, NRCOOR, $OCONR_2$, RCO, COOR, alkyl-OOCR, SO_3R, $CONR_2$, SO_2NR_2, $NRSO_2NR_2$, CN, CF_3, R_3Si, and NO_2, wherein each R is independently H, alkyl, alkenyl or aryl or heteroforms thereof and two of R^4 on adjacent positions can be joined to form a fused, optionally

substituted aromatic or nonaromatic, saturated or unsaturated ring which contains 3-8 members, or R^4 is =O or an oxime, oximeether, oximeester or ketal thereof;

m is 0-4;

Ar^2 is ~~a substantially planar, monocyclic or polycyclic aromatic moiety having one or more optional ring heteroatoms, said moiety being optionally substituted with one or more non-interfering substituents, two or more of which may form a fused ring~~ phenyl,



H is N or CR

wherein R is hydrogen or

(a) alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, NH-aroyl and halo; or

(b) or OR, NR_2, SR, SOR, SO_2R, OCOR, NRCOR, $NRCONR_2$, NRCOOR, $OCONR_2$, RCO, COOR, alkyl-OOCR, SO_3R, $CONR_2$, SO_2NR_2, $NRSO_2NR_2$, CN, CF_3, R_3Si, and NO_2, wherein each R in the preceding (b) selections is independently H, alkyl, alkenyl or aryl or heteroforms thereof;

and wherein two R can be joined to form a fused, optionally substituted aromatic or nonaromatic, saturated or unsaturated ring which contains 3-8 members;

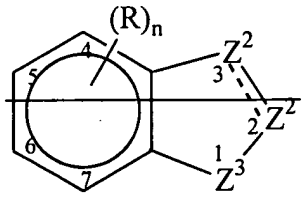
Z is $-W_i-COX_jY$ wherein Y is COR^3 or ~~an isostere thereof~~ tetrazole; 1,2,3-triazole; 1,2,4-triazole; or imidazole; R^3 is ~~[[a]]~~ an H or a noninterfering substituent which is straight or branched chain alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroalkyl, heteroaryl, or heteroarylalkyl, each optionally substituted with halo, alkyl, heteroalkyl, SR, SOR, SO_2R, SO_2NR_2, OR, NR_2, OCOR, NRCOR, $NRCONR_2$, $NRSO_2R$, $NRSO_2NR_2$, $OCONR_2$, CN, COOR, $CONR_2$, COR, or R_3Si wherein each R is independently H, alkyl, alkenyl or aryl or the heteroatom-containing forms thereof, or

wherein R^3 is OR, NR_2, SR, $NRCONR_2$, $OCONR_2$, or $NRSO_2NR_2$, wherein each R is independently H, alkyl, alkenyl or aryl or the heteroatom-containing forms thereof, and wherein two R attached to the same atom may form a 3-8 member carbocyclic or heterocyclic ring and wherein said ring may further be substituted by alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroalkyl, heteroaryl, heteroarylalkyl, each optionally substituted with halo, SR, OR, NR_2, OCOR, NRCOR, $NRCONR_2$, $NRSO_2R$, $NRSO_2NR_2$, $OCONR_2$, or R_3Si wherein each R is independently H, alkyl, alkenyl or aryl or the heteroatom-containing forms thereof wherein two R attached to the same atom may form a 3-8 member ring, optionally substituted as above defined,

each of W and X is ~~a spacer~~ an alkylene of 2-6 Å, and each of i and j is independently 0 or 1;

~~wherein the distance in space between the atom of Ar^1 bonded to L^2 and the atom of Ar^2 bonded to L^1 is is no more than 24 angstroms;~~

~~with the proviso that the portion of the compound represented by Ar^2-Z is not~~



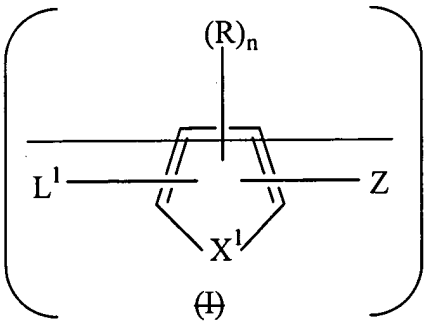
~~wherein~~ ~~represents a single or double bond; n is 0-3; one Z^2 is CA or CRA and the other is CR, CR_2, NR or N; A is $-W_i-COX_jY$ wherein Y is COR or an isostere thereof, each of W and X is a spacer of 2-6Å, and each of i and j is independently 0 or 1; Z^3 is NR or O; and each R is independently hydrogen or a noninterfering substituent.~~

2-5. (canceled)

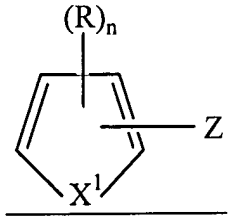
6. (original): The compound of claim 1 wherein each of i and j is 0.

7-9. (canceled)

10. (currently amended): The compound of ~~claim 8~~ claim 1 wherein the portion of said compound represented by ~~[[L^1-Ar^2-Z]]~~ Ar^2-Z is selected from the following:

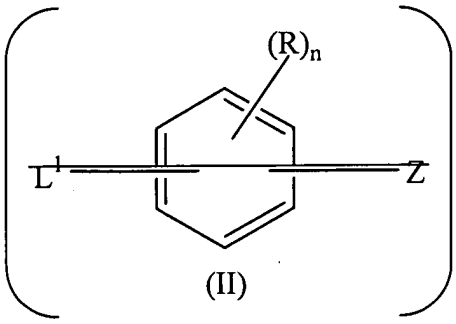


~~(I)~~

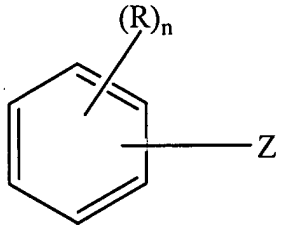


(I)

wherein n is 0, 1 or 2; X^1 is NR[[,]] or CR_2[[, ~~O or S~~]]; and each R is independently H or a noninterfering substituent; and two or more R groups may form a fused ring;

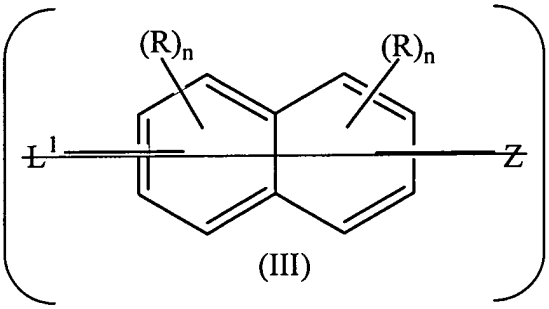


(II)

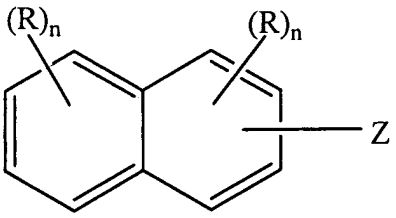


(II)

wherein n is 0-4; R is H or a noninterfering substituent where two or more R groups may form a fused ring; and one or more ring carbons may be optionally replaced with nitrogen;

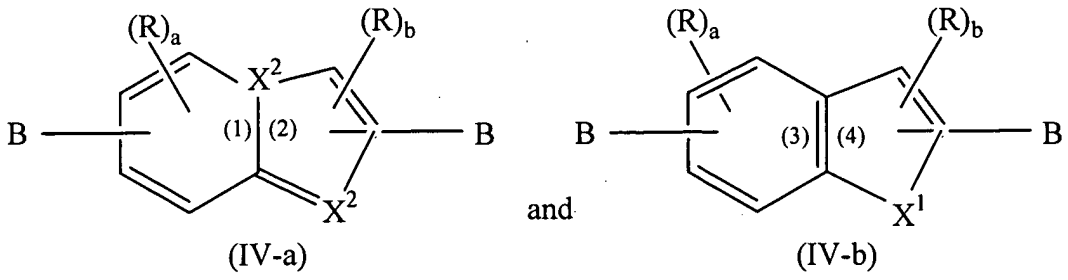


(III)

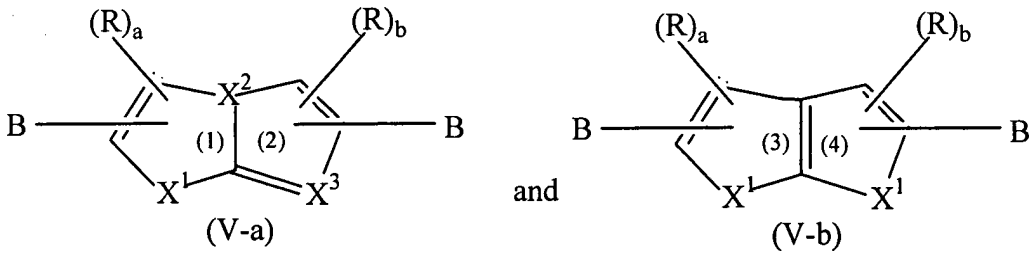


(III)

wherein each n is independently 0 to 3; R is H or a noninterfering substituent, where two or more R groups may form a fused ring; and one or more ring carbons may be optionally replaced with nitrogen;



wherein~~, subject to the proviso of claim 1,~~ one B is [[~~L~~$^+$]] CO and the other is Z; wherein a is 0 to 4 such that the positions on the six membered rings (1) and (3) to which $(R)_a$ is bonded can include X^2 when X^2 is C; b is 0–3 such that the positions on the five-membered rings (2) and (4) to which $(R)_b$ is bonded can include X^2 and X^1, when X^2 is C and X^1 is N or C; each X^2 is independently N or CR; X^1 is NR[[~~,~~]] or CR_2[[~~, O or S~~]]; each R is H or a noninterfering substituent where two or more R groups may form a fused ring; wherein one or more of the ring carbons that are at positions other than X^2 or X^1 and that are also not bound to B can be optionally replaced with N;

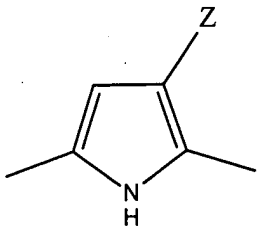


wherein one B is [[~~L~~$^+$]] CO and the other is Z; a is 0-4 such that the positions on the rings (1) and (3) to which $(R)_a$ can be bonded include X^2 and X^1 where X^2 is C and X^1 is C or N; b is 0 or 3 such that the positions on the rings (2) and (4) to which $(R)_b$ can be bonded include X^1, X^2 and X^3 when X^1 is C or N and X^2 and/or X^3 are C; each X^1 is independently NR[[~~,~~]] or $C(R)_2$[[~~, O or S~~]]; X^2 and X^3 are independently N or CR; each R is independently H or a noninterfering substituent where two or more R groups can optionally form a fused ring; wherein one or more of the ring carbons that are at positions other than X^1, X^2 or X^3, and that are also not bound to B, can be optionally replaced with N;

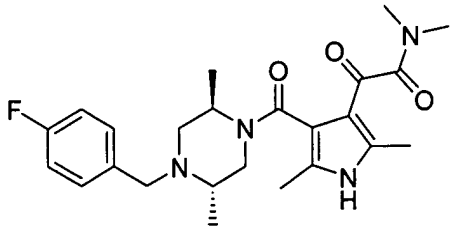
wherein each non-interfering substituent is independently selected from the group consisting of H, alkyl, acyl, aryl, arylalkyl, heteroalkyl, heteroaryl, halo, OR, NR_2, SR, NRCOR, alkyl-OOCR, RCO, COOR, and CN, wherein each R is independently H, alkyl, or aryl or heteroforms thereof.

11-15. (canceled)

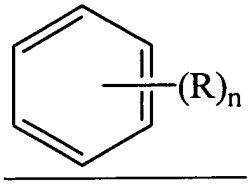
16. (currently amended): The compound of ~~claim 15~~ claim 1 wherein ~~structure (I)~~ Ar^2-Z is:



17. (previously presented): The compound of claim 16 where the compound is:



18. (currently amended): The compound of ~~claim 10~~ claim 1 wherein [[~~L^1-Ar^2-Z~~]] Ar^2-Z is ~~structure (II)~~:

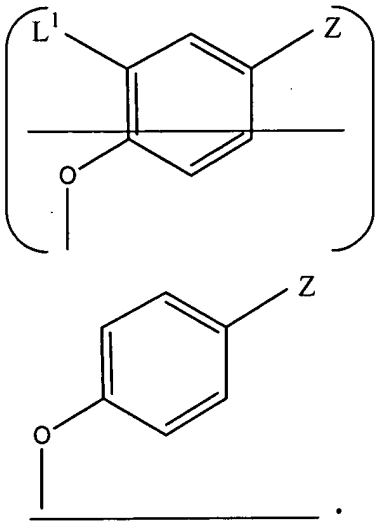


wherein n is 0-4.

19. (currently amended): The compound of claim 18 wherein [[~~the~~]] each R ~~in structure (II)~~ is methoxy.

20. (currently amended): The compound of claim 19 wherein n ~~in structure (II)~~ is 1.

21. (currently amended): The compound of ~~claim 20~~ claim 10 wherein structure (II) is



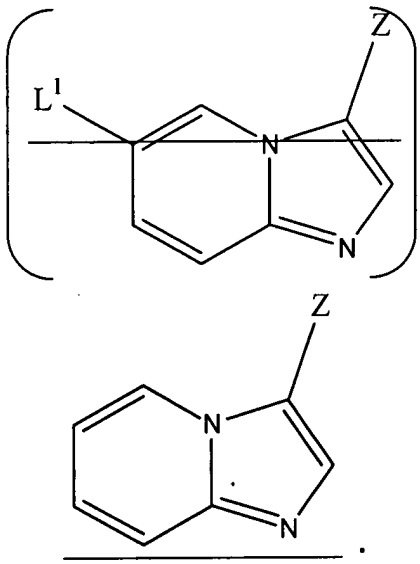
22. (canceled)

23. (currently amended): The compound of claim 10 wherein ~~[[L1-Ar2-Z]]~~ Ar2-Z is structure (III).

24. (currently amended): The compound of claim 10 wherein ~~[[L1-Ar2-Z]]~~ Ar2-Z is structure (IV-a) or (IV-b).

25. (currently amended): The compound of claim 24 wherein ~~[[L1-Ar2-Z]]~~ Ar2-Z is (IV-a) and both X^2 in structure (IV-a) are nitrogen.

26. (currently amended): The compound of claim 25 wherein structure (IV) is:



27. (canceled)

28. (currently amended): The compound of ~~claim 8~~ claim 10 wherein [[~~L~~^{1}-~~Ar~~^{2}-~~Z~~]] Ar^2-Z is structure (V-a) or (V-b).

29. (currently amended): The compound of claim 28 wherein [[~~L~~^{1}-~~Ar~~^{2}-~~Z~~]] Ar^2-Z is structure (V-a) and X^2 and X^3 in structure (V-a) are N.

30. (original): The compound of claim 29 wherein at least one R in structure (V) is methyl.

31-42. (canceled)

43. (currently amended): The compound of ~~claim 42~~ claim 1 wherein Ar^1 is optionally substituted phenyl.

44. (original): The compound of claim 43 wherein said optional substitution is by halo, OR, or alkyl.

45. (original): The compound of claim 44 wherein said phenyl is unsubstituted or has a single substituent.

46. (canceled)

47. (currently amended): The compound of ~~claim 46~~ claim 1 wherein each R^1 is halo, OR, or alkyl.

48. (original): The compound of claim 47 wherein m is 0, 1, or 2.

49. (original): The compound of claim 48 wherein m is 2 and both R^1 are alkyl.

50. (canceled)

51. (currently amended): The compound of ~~claim 50~~ claim 1 wherein the non-interfering groups are independently selected from the group consisting of H, alkyl, acyl, aryl, arylalkyl, heteroalkyl, heteroaryl, halo, OR, NR_2, SR, NRCOR, alkyl-OOCR, RCO, COOR, and CN, wherein each R is independently H, alkyl, or aryl or heteroforms thereof.

52. (canceled)

53. (previously presented): A pharmaceutical composition for treating conditions characterized by enhanced p38-α activity which composition comprises

a therapeutically effective amount of a compound of claim 1

along with a pharmaceutically acceptable excipient.

54-56. (canceled)

57. (withdrawn): A method to treat a condition mediated by p38-α kinase comprising administering to a subject in need of such treatment a compound of claim 1 or a pharmaceutical composition thereof.

58. (canceled)

59. (withdrawn): The method of claim 57 wherein said condition is a proinflammation response.

60. (withdrawn): The method of claim 59 wherein said proinflammation response is multiple sclerosis, IBD, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, gouty arthritis, other arthritic conditions, sepsis, endotoxic shock, asthma, adult respiratory distress syndrome, reperfusion injury, psoriasis, cerebral malaria, chronic pulmonary inflammatory disease, silicosis, pulmonary sarcosis, a bone resorption disease, graft-versus-host reaction, Crohn's Disease, ulcerative colitis, or pyresis.